

Growth Factors/Cytokines for White Blood Cells

Cytokine	Adult Dose	Pregnant Women
G-CSF: filgrastim (Neupogen®)	<ul style="list-style-type: none"> Subcutaneous administration 5 ug/kg/day via single daily injection Continued until absolute neutrophil count > 1.0 x 10⁹ cells/L 	Class C (Same as adults)
Pegylated G-CSF: pegfilgrastim (Neulasta®)	<ul style="list-style-type: none"> 1 subcutaneous dose, 6 mg Consider second 6 mg dose 7 or more days after initial dose, if significant neutropenia persists 	Class C (Same as adults)
GM-CSF: sargramostim (Leukine®)	<ul style="list-style-type: none"> Subcutaneous administration 250 ug/m²/day Continued until absolute neutrophil count > 1.0 x 10⁹ cells/L 	Class C (Same as adults)

G-CSF = granulocyte colony-stimulating factor; GM-CSF = granulocyte-macrophage colony-stimulating factor.

General comments:

- Consult hyperlinks in the first column of the table for important drug information.
- See REMM [Exposure Algorithm](#) for the clinical context of cytokine use
- The need for myeloid cytokines can be estimated using [biodosimetry tools](#)
- Initiation of treatment should be strongly considered for victims who
 - Are likely to have received ≥ 2 [Gy](#) whole body exposure or ≥ 2 [Gy](#) significant partial body exposure
 - Are likely to develop an absolute neutrophil count of $< 0.500 \times 10^9$ cells/L
 - Will likely have prolonged periods of significant neutropenia ([See diagram.](#))
 - Have significant radiation exposure plus trauma and/or burns
- The goal of using cytokines is to
 - Shorten the duration of severe neutropenia
 - Minimize the severity of neutropenia-associated complications
- Most experts recommend using white cell cytokines **as early as possible and usually within 24 hours after the end of radiation exposure.**
 - These timing data are based mostly on evidence from animal studies.¹
- In a large mass casualty radiation incident such as a nuclear detonation
 - There may be significant shortages of resources including white cell cytokines.

- Consult [REMM's Interactive Tool](#) to assist with triage and allocation of scarce resources including these cytokines in the first 96 hours of an IND detonation.
- Although the 3 drugs listed in the table above are FDA approved for the treatment of chemotherapy induced neutropenia, none is approved for radiation induced neutropenia.
 - No prospective randomized trials have proven either the efficacy or long term safety of hematopoietic growth factors in humans exposed to radiation.
 - However, experience using white cell cytokines after accidental radiation exposure has been gained during incidents involving small numbers of patients, as tracked by [REAC/TS](#), and in smaller clinical studies.
 - Procurement and use of these drugs from the [Strategic National Stockpile](#) would require a formal [Emergency Use Authorization \(EUA\)](#).
 - In a large mass casualty event, off label use by individual clinicians might occur from sources outside the SNS, but FDA still recommends an EUA. Incident managers will probably provide direction on this issue during a mass casualty event.
- For radiation exposure in pregnant women and cytokines use
 - Experts in biodosimetry must be consulted.
 - Any pregnant patient with exposure to radiation should be evaluated by a health physicist and maternal-fetal specialist for an assessment of risk to the fetus.
 - **Class C** refers to U.S. Food and Drug Administration Pregnancy Category C, which indicates that studies have shown animal, teratogenic, or embryocidal effects, but there are no adequate controlled studies in women; or no studies are available in animals or pregnant women.
 - [See recent FDA update for use of cytokines in pregnancy](#)
- See practice guidelines for myeloid growth factors from
 - [National Comprehensive Cancer Network](#) (Registration required to view this content entitled "Myeloid Growth Factors")
 - [American Society of Clinical Oncology](#) (2006)

Additional issues/warning suggested by REMM consultants:

- Safety and efficacy of growth factors in **pediatric patients** have not been established; however, available safety data for some of the growth factors (e.g., GM-CSF) indicate that this particular growth factor does not produce any greater toxicity in pediatric

patients than in adults. [Emergency use authorization](#) would be required in a mass casualty event.

- Daily G-CSF (filgrastim and pegfilgrastim) therapy leads to splenic enlargement in a very small fraction of patients, and very rare cases of splenic rupture have been documented.
- Allergic reactions involving skin, respiratory, and cardiovascular symptoms have been reported in patients administered filgrastim and pegfilgrastim. Although these side effects have occurred at a relatively low rate (<1 in 4000 patients for filgrastim), in a large scale radiological incident there may be patients who experience this side effect.

